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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,555	01/19/2001	Carlos F. Barbas III	278012001420	1190

25225 7590 09/09/2005

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EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,555	BARBAS ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-8, 11, 13-16, 18-22, 28-30, 36-44, 46, 48, 50-59, 61-66, 70-72, 74, 76-78, 83, 85, 88, 91-95, 98-100, and 133-137* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice To Comply Sequence Rules

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DETAILED ACTION

Receipt is acknowledged of Applicants' response to the final Office action mailed 02/23/05. However, upon further search and consideration, it has been determined that the finality of the rejection of the last Office action be withdrawn. The Office action contains NEW GROUNDS OF REJECTIONS and is made non-final. Any inconvenience the delay may have caused Applicant is deeply regretted.

Applicant's response of 06/15/05 has been considered.

Claims 1, 4-8, 11, 13-16, 18-22, 28-30, 36-44, 46, 48, 50-59, 61-66, 70-72, 74, 76-78, 83, 85, 88, 91-95, 98-100, and 133-137 are pending and are under consideration.

Sequence Listing

Applicant's CRF and paper sequence listing filed 12/16/04 have been entered. However, this application fails to comply with the requirements of 37 CFR 1.821-1.825. Nucleotide and /or amino acid sequences as used in §1.821 through 1.825 are interpreted to mean unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides in patent applications. The 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. In this application, the peptide sequence on page 32, line 1, of the specification and the motif sequences of "QALGGH" in claim 137 have not been identified by SEQ ID NO: Applicant is respectfully requested to identify the sequences

on page 32 and in claim 137 or to submit a new Sequence Listing, which comprises said sequences. The specification and the claim should also be amended to recite the SEQ ID NO: See attached Notice to Comply.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-8, 11, 13-16, 18-22, 28-30, 36-44, 48, 50, 51-59, 61-66, 70-72, 74, 76-78, 83, 85, 88, 91-95, 98-100, and 133-137 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 70 and 74 are indefinite in the recitation of "mutations at one or more of the base contacting positions" which is a relative description lacking comparative basis. It is unclear whether the mutation is relative to its wild type ZFP or to another unknown synthetic ZFP. One would not know the metes and bounds of the claims. Dependent claims 5-8, 11, 13-16, 18-22, 28-30, 36-44, 48, 50, 51-59, 61-66, 71-72, 76-78, 83, 85, 88, 91-95, 98-100, and 133-137 are included in the rejection because they do not obviate the rejection.

Claims 1, 4, 36, 70 and 74 are indefinite because if the target nucleotide is of the formula (GNN)6, the complementary strand of the target sequence would not be of the same formula. Clarification is required to more clearly define the metes and bounds of the claims.

Claim 7, depending from claim 1, is indefinite in the recitation of "wherein the target nucleotide sequence is DNA, RNA, PNA or a combination thereof". Claim 1 recites that the zinc finger is a "DNA" binding protein rather than "DNA, RNA, PNA or combination thereof" binding protein. Clarification is required to more clearly define the metes and bounds of the claim.

Claim 14, depending from claim 1, is indefinite in the recitation of " different target nucleotide sequences". Claim 1 recites that the target nucleotide sequence is of the formula (GNN)6. the specification does not define what is encompassed by a different target nucleotide sequence. Clarification is required to more clearly define the metes and bounds of the claim.

Claims 46 and 74 are indefinite in the recitation "ZFPm1, ZFPm2, ZFPm4 and ZFPAp3". Since the name "ZFPm1, ZFPm2, ZFPm4 and ZFPAp3" are not known in the art, the use of said name does not carry art-recognized limitations as to the specific or essential characteristics that are associated with that denomination. The name "ZFPm1, ZFPm2, ZFPm4 and ZFPAp3" does not clearly identify the synthetic zinc finger protein of the claimed invention, and does not set forth the metes and bounds of the claimed invention. The name appears to have been arbitrarily assigned and can be changed. The specific characteristics associated therewith can also be modified. Amending claims 46 and 74 to recite SEQ ID NO: would overcome the rejection. Dependent claims 76-78, 83, 85, 88, 91-95, 98-100 are included in the rejection because they do not obviate the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-8, 13-16,19-20, 22, 28-29, 36-43, 48, 50, 50-59, 70, and 133-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cox, III et al (US 6, 534, 261, filed January 1999) in view of Segal et al (Proc. Natl. Acad. Sci. USA (1999) 96:2758-2763, Applicant's IDS).

Claims are drawn to a method for modulating gene expression in plant/plant cells comprising transforming plant cells with an expression vector comprising a nucleotide sequence encoding a hexadactyl zinc finger protein that specifically binds to a target nucleotide sequence or a complementary strand thereof of the target gene, wherein the

target nucleotide sequence is of the formula (GNN)6, where N is A, T, C, G, wherein the zinc finger protein comprises one individual zinc finger with DNA binding site with mutation at one or more of the base-contacting positions, and culturing/regenerating the plant cells under conditions such that the zinc finger protein is stably expressed in said plant cell/plant, whereby the expression of the target gene in the plant/plant cell is stably modulated, and wherein the modulation is either repression or activation. The claims also encompass said method wherein the target sequence is upstream, downstream or within the coding region of the target gene and is endogenous or exogenous to the plant/cell or, and wherein the target gene encodes a protein/peptide, an enzyme, a transport protein, a nutrient protein, a storage protein, an antibody, a defense protein or regulatory protein. The claims also encompass said method wherein the zinc finger protein specifically binds to an effector domain and comprises a plurality of finger regions separated by linker region with from 2 to 10 amino acid residues in length, and wherein the zinc finger protein comprises a framework from a plant zinc finger protein or comprises C3H zinc finger or C2H2 motif.

Cox, III et al teach methods of modulating expression level of cellular genes in plant cells by transforming the plant cells with an expression vector comprising a nucleic acid sequence encoding a synthetic zinc finger protein (sZFP) under the control of a constitutive, inducible or tissue-specific promoter (see at least columns 35-36; column 5, lines 4-8; column 1, lines 54-65, columns 15-16, and claims). The cited reference teaches a nucleic acid encoding 6-finger zinc finger protein that effectively modulate the expression level of an endogenous gene (SEQ ID NO: 29; column 7, lines 48-50;

column 44, lines 34-65). The cited reference also teaches that the ZFPs are designed from a backbone of C2H2 ZFPs including SP-1, SP-1C and Zif268 which bind a target nucleotide sequence with 18 contiguous bases, and that the target site can be upstream, downstream or within the coding region of a target gene, and that the ZFP is mutagenized in regions important for binding or affinity (columns 15-16, 24-25, and claims). Cox, III et al teach the use of linker peptides with 5 to 100 amino acids to link two three-finger proteins (column 23, lines 31-54). At columns 35-36, the cited reference teaches regulation of gene expression in plant/plant cells with said synthetic ZFPs in order to modify a desired trait such as increasing disease resistance or modification of seed oils. The cited reference teaches that nucleic acids encoding sZFPs are used to transform soybeans to inhibit expression of FAD2-1 gene in order to increase the accumulation of oleic acid in the oil seed (column 36, lines 15-34). The cited reference also teaches several techniques for plant transformation, and methods for plant regeneration from cultured protoplasts (column 37). The cited reference further teaches that the expression of target gene may be increased by 7-10 fold or decreased by 40-50 fold by using a repressor or activator domain fused to the ZFP (columns 17 and 51-53, Examples VI-VII).

While Cox, III et al teach ZFP that binds to 18 contiguous bases, Cox III, et al do not explicitly teach 18 contiguous bases with (GNN)6 sequence.

Segal et al teach selection and design of zinc finger proteins that bind (GNN)6 target sequence, and its use for a universal system for gene control (pages 2759-2760, Results and Discussion).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the method of modulating gene expression in plant/plant cells with a 6- zinc finger protein encoding nucleic acid as taught by Cox, III et al, and to modify that method by incorporating a 6-zinc finger protein that recognizes (GNN)6 sequences, given that majority of synthetic polydactyl ZFPs are capable pf recognizing 18 bp with (GNN)6 nucleotide sequence. One of ordinary skill in the art would have been motivated to use a 6-designed zinc finger protein given that a 6-zinc finger protein is known to effectively binds 18 bp and modulates expression of cellular genes as taught by Cox, III et al. One of ordinary skill in the art would have been motivated to use more than one copy of 6-designed zinc finger protein to effectively bind more than one target nucleotide sequences within the target gene, given the successful results with one 6-finger zinc protein. One would have had a reasonable expectation of success in carrying out the claimed invention as taught by Cox et al. In addition, methods of stably transforming plants with heterologous genes are known in the art as suggested by Cox III, et al.

Claims 1, 4-8, 13-16,19-20, 22, 28-29, 36-43, 50, 48, 50-59, 61-66, 70, and 133-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cox, III et al (US 6, 534, 261, filed January 1999) in view of Segal et al (Proc. Natl. Acad. Sci. USA (1999) 96:2758-2763, Applicant's IDS) as it applies to claims 1, 4-8, 13-16, 19-20, 22, 28-29, 36-43, 50, 48, 50-59, 70, and 133-137 above, and further in view of Applicants' admitted prior art.

Cox, III et al in view of Segal do not explicitly teach the inclusion of a transit peptide in the plant expression vector. However, the inclusion of a transit peptide that targets a desired protein to specific organelle of a plant in a plant transformation vector was well known in the prior art, as evidenced by Applicant's own specification (page 63, lines 8-27).

Applicant's admitted prior art indicates that chloroplast, mitochondria and nucleus transit peptides were well known and widely used at the time Applicant's invention was filed.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize any of the known transit peptide sequences of the prior art, including the claimed chloroplast, mitochondria and nucleus transit peptides for their availability, in the transformation vector without any unexpected results. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Therefore, the claimed invention as whole was a prima facie obvious.

1. Claims 1, 4-8, 11,13-16,19-22, 28-30, 36-44, and 133-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE Pater Sylvia et al (nucleic Acids Research, vol. 24 (23), pp. 4624-4631, 1996, in the record.) in view of BARBAS et al (WO 9854311, Applicant's IDS).

DE Pater Sylvia et al teach a method of activating gene expression in plant cells with ZAP1, zinc finger protein from Arabidopsis with transcriptional enhancing activity; the method comprising introducing an expression construct comprising ZAP1 cDNA under the control of a 35S promoter into Catharanthus roseus cells together with a reporter construct comprising gus under the control of a truncated 35S promoter fused to synthetic ZAP1 binding sites (page 4626, Materials and Methods; Figure 5). Results show that the expression of ZAP1 protein in the plant cells increased transcription level of GUS by 6 fold (Figure 10B and C). Results further show that ZAP1 functions as a sequence-specific zinc finger protein type of transcriptional activator in plant cells (page 4628). The results further show the sequence CGTTGACCGAG as the optimal binding site for ZAP1, which implies that ZAP1 can impose transcriptional activation an all target genes with said optimal sequence in the promoter region, such genes are barley alpha amylase and maize pathogen related PRms genes (page 4632, column 1).

DE Pater Sylvia et al do not teach a method that employs non-natural zinc finger proteins to control gene expression in plant cells and plant.

BARBAS et al disclose a plant expression vector comprising a nucleotide sequence encoding a synthetic 6-zinc finger protein operably linked to CaMV (constitutive) or hsp (inducible) promoter (page 38, first full paragraph) and suggests that the designed zinc finger proteins can be used to modulate expression of a target gene in plant cells (claim 18) to produce transgenic plants with a desired phenotype such as disease resistant transgenic plants by using methods known in the art (page 38, lines 3-15; page 48, lines 3-8; page 49, lines 12-16) . The cited reference teaches

methods for designing two six finger proteins (C7-C7 linked by TGEKP peptide, and a Sp1C-C7) derived from wild type zinc finger proteins such as Zif268 and TFIIIA known in the art, that bind 18 bp with (GNN)6 sequence. The cited reference further teaches construction and designing zinc finger proteins comprising from 2 to 20 zinc fingers separated by linkers, and capable of binding to a cellular nucleotide sequence (DNA or RNA) in a target gene to modulate (activate or repress) the transcriptional activity of the gene (Examples 1-14). The cited reference teaches zinc finger proteins with mutations at base contacting sites with higher affinity and specificity to its binding sites as compared to zinc fingers with non-mutated base-contacting site (page 86, lines 5-16; page 91, lines pages 12, 21 and 30). At page 96, the cited reference teaches construction of 6-finger zinc finger protein fused with an activator domain resulted more than 300-fold stimulation of expression in living cells and that such construct can be used to transform plant cells. BARBAS suggests that any of the wild type zinc finger proteins known in the art can be used with his method to design novel zinc finger proteins that bind any chosen DNA sequence (paragraph bridging pages 2 and 3; page 16). Given the broad applicability of the method as taught by BARBAS, the expression of any target gene encoding a heterologous protein including those listed in instant claims 21, 29-30 in a plant or plant cell is expected to be affected by a suitable zinc finger protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the method of controlling gene expression in plant/plant cells with zinc finger protein as taught by DE Pater Sylvia, and to modify that method by

incorporating either the designed zinc finger proteins taught by BARBAS, or those obtainable from the wild type zinc finger proteins taught by DE Pater Sylvia, by using the zinc finger protein design and selection methods taught by BARBAS. One of ordinary skill in the art would have been motivated to use design zinc finger proteins instead of wild type because BARBAS teaches the advantage of using designed zinc finger proteins (higher degree of specificity sufficient for being selective even within a genome) in enhancing or repressing expression of endogenous cellular genes. One would have had a reasonable expectation of success in carrying out the claimed invention as taught by DE Pater Sylvia. One of ordinary skill in the art would have been motivated to use more than one copy of 6-designed zinc finger protein to effectively bind more than one target nucleotide sequences within the target gene for effective gene modulation, given the successful results with one 6-finger zinc protein. One would have had a reasonable expectation of success in carrying out the claimed invention as taught by DE Pater Sylvia. In addition, methods of stably transforming plants with heterologous genes are known in the art as suggested by BARBAS.

Claims 1, 4-8, 13-16,19-22, 28-30, 36-44, 51-59, 61-66, 70, and 133-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cox, III et al (US 6, 534, 261, filed January 1999) in view of Segal et al (Proc. Natl. Acad. Sci. USA (1999) 96:2758-2763, Applicant's IDS) as it applies to claims 1, 4-8, 11,13-16, 17, 19-22, 28-30, 36-44, 55-59, 70, and 133-137 above, and further in view of Applicants' admitted prior art.

The teaching of DE Pater Sylvia et al in view of BARBAS et al has been discussed above.

DE Pater Sylvia et al in view of BARBAS et al do not explicitly teach the inclusion of a transit peptide in the plant expression vector. However, the inclusion of a transit peptide that targets a desired protein to specific organelle of a plant in a plant transformation vector was well known in the prior art, as evidenced by Applicant's own specification (page 63, lines 8-27).

Applicant's admitted prior art indicates that chloroplast, mitochondria and nucleus transit peptides were well known and widely used at the time Applicant's invention was filed.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize any of the known transit peptide sequences of the prior art, including the claimed chloroplast, mitochondria and nucleus transit peptides for their availability, in the transformation vector without any unexpected results. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Therefore, the invention as a whole was *prima facie* obvious at the time the invention was made.

Claims 1, 4-8, 11,13-16, 19-22, 28-30, 36-44, and 133-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagisawa et al (The Plant Cell, vol. 10, pp. 75-89, 1998, in the record) in view of BARBAS et al (WO 9854311, Applicant's IDS).

Yanagisawa et al teach a method of controlling the expression of a gene in maize leaf tissues by using maize Dof1 zinc finger protein; the method comprises co-transforming maize plant cells with expression constructs comprising either, Dof cDNA and hsp promoter, or hsp promoter and Dof1 added to the activation domain GALA4, or the constitutive 35SC4PPDC (phosphoenolpyruvate carboxylase) gene promoter operably linked to Dof1, and a reporter plasmid construct comprising CAT and truncated 35 S with or without synthetic Dof1 binding site (see Page 77, and Figures 2-3; page 81, Figure 7). Results indicated that Dof1 binds specifically to the phosphoenolpyruvate carboxylase gene promoter in vitro and in vivo, and showed that Dof1 alone was sufficient to activate transcription by 5 fold (Figure 6; page 81). The addition of GALA in the transformation vector further increased the transcription by at least 1.5 fold. The results further showed that transcriptional activation by Dof1 was due to its selective binding to the target sequence (Figures 9 and 10). The cited reference teaches the structural and functional domains of Dof1 and Dof2 proteins, and a method of identifying their binding sites in the C4PEPC gene promoter (paragraph bridging pages 81 and 82). Yanagisawa et al have shown that Dof2 acts as a transcriptional repressor in plants, and that it can interact with Dof1 binding sites but lacks the activity for transcriptional activation (paragraph bridging pages 83 and 84, and Figure 11). These results indicate that the expression of a phosphoenolpyruvate carboxylase gene, can be regulated with the zinc finger protein Dof. A change of phenotype of transgenic plant/plant cell having modulated target protein is expected.

Yanagisawa et al do not teach a method that employs non-natural zinc finger proteins to control gene expression in plant cells and plant.

BARBAS et al disclose a plant expression vector comprising a nucleotide sequence encoding a synthetic 6-zinc finger protein operably linked to CaMV (constitutive) or hsp (inducible) promoter (page 38, first full paragraph) and suggests that the designed zinc finger proteins can be used to modulate expression of a target gene in plant cells (claim 18) to produce transgenic plants with a desired phenotype such as disease resistant transgenic plants by using methods known in the art (page 38, lines 3-15; page 48, lines 3-8; page 49, lines 12-16) . The cited reference teaches methods for designing two six finger proteins (C7-C7 linked by TGEKP peptide, and a Sp1C-C7) derived from wild type zinc finger proteins such as Zif268 and TFIIIA known in the art, that bind 18 bp with (GNN)6 sequence. The cited reference further teaches construction and designing zinc finger proteins comprising from 2 to 20 zinc fingers separated by linkers, and capable of binding to a cellular nucleotide sequence (DNA or RNA) in a target gene to modulate (activate or repress) the transcriptional activity of the gene (Examples 1-14). The cited reference teaches zinc finger proteins with mutations at base contacting sites with higher affinity and specificity to its binding site as compared to zinc fingers with non-mutated base-contacting site (page 86, lines 5-16; page 91, lines pages 12, 21 and 30). At page 96, the cited reference teaches construction of 6-finger zinc finger protein fused with an activator domain resulted more than 300-fold stimulation of expression in living cells and that such construct can be used to transform plant cells. BARBAS suggests that any of the wild type zinc finger

proteins known in the art can be used with his method to design novel zinc finger proteins that bind any chosen DNA sequence (paragraph bridging pages 2 and 3; page 16). Given the broad applicability of the method as taught by BARBAS, the expression of any target gene encoding a heterologous protein including those listed in instant claims 21, 29-30 in a plant or plant cell is expected to be modulated by a suitable zinc finger protein.

Claims 1, 4-8, 13-16,19-22, 28-30, 36-44, 51-59, 61-66, 70, and 133-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagisawa et al (The Plant Cell, vol. 10, pp. 75-89, 1998) in view of BARBAS et al (WO 9854311, Applicant's IDS).Cox, III et al (US 6, 534, 261, filed January 1999) as it applies to claims 1, 4-8, 11,13-16, 17, 19-22, 28-30, 36-44, and 133-137 above, and further in view of Applicants' admitted prior art.

The teaching of Yanagisawa et al in view of BARBAS et al has been discussed above.

Yanagisawa et al in view of BARBAS et al do not explicitly teach the inclusion of a transit peptide in the plant expression vector. However, the inclusion of a transit peptide that targets a desired protein to specific organelle of a plant in a plant transformation vector was well known in the prior art, as evidenced by Applicant's own specification (page 63, lines 8-27).

Applicant's admitted prior art indicates that chloroplast, mitochondria and nucleus transit peptides were well known and widely used at the time Applicant's invention was filed.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize any of the known transit peptide sequences of the prior art, including the claimed chloroplast, mitochondria and nucleus transit peptides for their availability, in the transformation vector without any unexpected results. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Therefore, the invention as a whole was *prima facie* obvious at the time the invention was made.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

8/30/05
Mai

MEDINA A. IBRAHIM
PATENT EXAMINER
1638

Notice to Comply	Application No. 09/765,555	Applicant(s) Barbas et al.	
	Examiner M. Ibrahim	Art Unit 1638	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: sequences on page 32 and in claim 137 lack sequence identifier, SEQ ID NO:.

Applicant Must Provide:

☒ An amended or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An amended or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
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Continuation of Disposition of Claims: Claims pending in the application are 1,4-8,11,13-16,18-22,28-30,36-44,46,48,50-59,61-66,70-72,74,76-78,83,85,88,91-95,98-100 and 133-137.